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Impact of Body Mass Index on short and long-term outcome after isolated first time surgical aortic valve replacement for aortic stenosis.

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Structured abstract:

Objective: To ascertain if body mass index (BMI) has a clinical impact on short and long term post-operative outcome after surgical aortic valve replacement in patients with severe aortic stenosis.

Design: Single centre retrospective study.

Setting: tertiary referral hospital.

Participants: 1561 patients underwent isolated first-time aortic valve replacement between 2005 and 2012.

Interventions: Fourteen underweight patients were removed from the analysis. The remaining patients were divided in 4 groups according to their BMI: 418 as normal weight (≥ 18.5 and < 25 kg/m^2), 629 as

overweight (≥ 25 and < 30 kg/m^2), 342 as obese (≥ 30 and < 35 kg/m^2) and 158 as very obese (≥ 35 kg/m^2). Early mortality and post-operative complications were compared, and long-term survival rates were investigated.

Measurement and main results: 30-day mortality was higher in the normal weight group, but did not reach statistical significance (p =0.054) and the incidence of postoperative complications was not different for cerebrovascular accident (p= 0.70), re-sternotomy for bleeding (0.17), sternal wound infection (p= 0.07) and dialysis (0.07). With a mean follow-up time of 4.92 ± 2.82 years, survival rate were better in the overweight group. A Cox Proportional Hazard Model found BMI inversely correlated with long-term mortality when analysed in a univariable fashion (HR: 0.95, p=0.009), but this apparent protective effect disappeared when adjusted for pre-operative co-variates (HR 0.98, 95% CI 0.96-1.004, p=0.12).

Conclusion: Once adjusted for pre-operative characteristics, obesity does not represent an independent predictor for long-term survival rates. There is a higher incidence of 30 days mortality in the normal weight group compared to overweight and very obese patients. The incidence of deep sternal wound infection is higher in the very obese patients.

Keywords: Obesity, Aortic Valve, Body Mass Index

Introduction

Obesity is rapidly becoming a problem of epidemic proportion in the western countries[1] and has almost doubled between 1998 and 2008[1] with around 35% of the population aged >20 years that was overweight[1]. Obesity and the metabolic syndrome are associated with adverse outcome[2] and are risk factors for several diseases including cardiovascular pathologies and malignancies[2]. Despite the fact that the lowest mortality in healthy population is at a Body Mass Index (BMI) between 22.5-25 Kg/m^2, several epidemiological studies have reported a survival benefit for overweight and obese patients and there is growing scientific evidence of a paradoxical effect of obesity and mortality[2]. The so-called “obesity paradox” has been demonstrated in several studies in different clinical settings like type 2 diabetes[3], cancer[4], chronic obstructive pulmonary disease[5] and cardiovascular diseases[1]. The underlying protective mechanism of the obesity paradox is uncertain, and its relevance appears to applies mostly to mildly overweight individuals[6]: moreover it has

been demonstrated that visceral adiposity is associated with cardiovascular risk, while subcutaneous fat accumulation is not[6].

The obesity paradox has also been described in valvular heart surgery where an elevated Body Mass Index (BMI) seems to have a positive impact on long term survival after valve surgery[7], although limited data with contrasting results are available after surgical aortic valve replacement[8,9,10]. A previously reported series did not support the evidence of such paradox in patients undergoing to aortic valve replacement[11] and showed that BMI is not independently associated with worsened short and long term outcomes after surgery. Instead, another retrospective study demonstrated a strong correlation between BMI and 30-day and long term mortality after aortic valve surgery[12].

Through a single centre retrospective analysis, we aimed to clarify the correlation between BMI and short outcomes and long-term survival after isolated surgical aortic valve replacement (AVR) for aortic stenosis.

Materials and methods

This is a retrospective single-centre study. Our internal cardiac surgery database was queried for any cardiac surgical operation that involved a surgical aortic valve replacement from May 2005 to December 2015 and 2302 patients met this criterion: we removed 82 patients that had other associated procedures, 410 patients that had aortic valve regurgitation as main diagnosis and 235 patients had previous cardiac surgery. In the remaining database, 14 patients did not have BMI data available and therefore had to be excluded. The final dataset comprises 1561 patients who had isolated first-time aortic valve replacement for aortic valve stenosis. These patients were stratified according to their BMI into 4 categories, as defined by the World Health Organization[13]: underweight (BMI < 18.5 kg/m^2), normal weight (BMI ≥ 18.5 and < 25 kg/m^2), over-weight (BMI ≥ 25 and < 30 kg/m^2), and obese (BMI ≥ 30 kg/m^2). A further stratification of the obese patients was conducted to differentiate the very obese patients (BMI ≥ 35 kg/m^2) form the obese patients (BMI ≥ 30 kg/m^2 and < 35 kg/m^2). The underweight group comprised only 14 patients and therefore was excluded from the analysis to avoid biases on the statistical methods. Clinical characteristics, symptoms status, operative and postoperative data were obtained from our cardiac surgery database (Patient Analysis & Tracking System, Dendrite Clinical Systems, Henley-on-Thames, UK) and were prospectively collected during the admission of the patients. Aortic valve prosthesis selection and implantation technique were

according to surgeon preference. The survival data were obtained from our internal database or from the UK National Health Service (NHS) tracing service if missing in our database: the latest data collection was obtained in July 2016. Euroscore was calculated accordingly to established method[14]. The primary endpoint was long-term all-cause mortality. The secondary endpoints were 30 days mortality, in hospital complications and length of stay (LOS).

Re-operation for bleeding was defined as a new sternotomy due to excessive post-operative bleeding and its indication was decided by the responsible operative surgeon. Post-operative cerebro-vascular accident (CVA) consisted of any new stroke identified clinically and/or by CT scan. Occurrence of acute kidney injury (AKI) was defined as need for post-operative new hemofiltration/dialysis. Deep sternal wound infection (DSWI) was defined as an infection of the sternal wound with positive culture results or drainage from the mediastinal area or evidence of infection during surgical re-exploration or fever, sternal instability, and positive blood culture results. The local audit committee approved the study, and the requirement for individual patient consent was waived. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

Continuous variables are reported according to their distribution with mean ± standard deviation if normally distributed and median and interquartile range (IQR) if not normally distributed. Normality was assessed with Lilliefors test. Categorical variables are reported as count and frequencies. When comparing preoperative characteristics, operative characteristics and postoperative outcomes, the Kruskal–Wallis test was used for continuous variables while the Chi-square test was used for categorical variables. Simple linear regression models were run to study the correlation between BMI and operative surgical times and post-operative length of stay. Long-term survivals for each group are presented as the Kaplan–Meier survival curves, and the log-rank test was used to compare the curves. Effects of the clinical variables on long-term survival were assessed using univariable and multivariable Cox proportional hazard models. The multivariable Cox model was fitted including the variables that were significantly associated with late mortality in the univariable model (age, diabetes, hypertension, New York Heart Association Class > II, previous myocardial infarction, chronic obstructive pulmonary disease, pre-operative atrial fibrillation, reduced left ventricular ejection fraction and Euroscore). We also analysed the association of BMI as a

continuous variable to the risk of all-cause long-term mortality using a Cox regression model with restricted cubic spline function (k = 4[15]). All tests were two sided and alpha error was set at 0.05. The statistical analysis was conducted in R version 3.5.0 (2018-04-23) (R Core Team (2018). R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/)

Results

The mean age for the entire population was 70.2 ± 11.2 years and 44% of the patients were female. The mean additive Euroscore was 5 ± 2.4 , while mean Logistic Euroscore was 6±5% . BMI ranged between 18.6 and 53.9 kg/m^2 with a mean value of 28.3±5.1 kg/m^2 : 418 patients(27 %) were classified as normal weight, 629 (40.1%) as overweight, 342 (22.1%) as obese and 158(10.2%) as very obese. **Table 1** shows the demographic and pre-operative characteristics of the patients. A linear model found a significant inverse correlation between BMI and age (Adj R^2=0.014, $p < 0.01$). The median cardiopulmonary bypass time was 91 minutes (IQR 78-107) while the median cross-clamp time was 67 minutes (IQR 57-79).. A simple linear regression models found a significant association between CPB time and BMI (Adj R^2=0.002, p=0.03) but not between cross-clamp time and BMI (Adj R^2= 0.0008, p = 0.12). **Table 2** shows post-operative outcomes. The overall 30-days mortality rate was 1.4 % with the highest rate recorded in the normal weight group (2.6%) and no early mortality events recorded in the very obese group. . The presence of a deep sternal wound infection was more frequent in the very obese group (1.9%), although there was no significant difference compared to the other groups (p=0.07). The median post-operative length of stay was 7 days with the longest length of stay measured in the very obese group (Median 8 days, IQR 6-10) and no significant differences between the groups; there was no significant correlation between BMI and length of stay (p = 0.6).

Figure 1 displays the Kaplan-Meier curves for each group. The mean follow-up time was 4.92 ± 2.81 years: during this period a total of 326 deaths were recorded. At one year the survival rates were 93.5% for the normal weight group, 97.6% for the overweight group, 94.7% for the obese group and 98.1 for the very obese group. At five years the survival rates were 77.9% vs 84.9% vs 82.7% vs 87% while at 10 years they were 46.7% vs 68.6% vs 53 % vs 64.3% respectively. The mortality rate was 0.55, 0.36, 0.45 and 0.36 per

10 years of person-time for underweight, normal, overweight, and obese patients, respectively. When analysed as a categorical variable, BMI group appeared to significantly affect the long-term survival. Compared to normal weight patients, the overweight group had the lowest risk of death with an HR of 0.63 (95% CI 0.48-0.81, p= < 0.01) while very obese patients had a HR 0.64, (95% CI: 0.42-0.96, p < 0.03). No significant difference was found for the obese patients, although the HR was still in favour of this group compared to normal weight patients (HR 0.81, 95% CI 0.60-1.09, p = 0.17). When adjusted for co-variates, only the overweight group had a significant better survival hazard ratio (HR 0.67, 95% CI: 0.51-0.88, p = 0.004). Similar results were found when using BMI as a continuous linear variable: at univariable analysis the HR was 0.95 (95% CI: 0.94-0.99) with a significant p value (p=0.009), while in a multivariable model adjusted for co-variates, BMI did not impact significantly on the long-term survival rates (adjusted HR: 0.98, 95% CI 0.96-1.004, p=0.12). **Table 3** shows the results of the Univariable and Multivariable Cox proportional hazard model.

Figure 2 shows the estimated log HR for BMI (with restricted cubic spline function) in univariable and multivariable Cox Proportional Hazard models:When adjusted for covariates, the apparent benefit showed in the univariable analysis is not anymore evident and the hazard ratio remains stable in the overweight and obese patients.

Discussion

Our study proves that an obesity paradox in surgical aortic valve replacement is only apparent and the adjusted hazard ratio demonstrates that there is a significant influence of other pre-operative covariates on the long-term survival of obese and very obese patients. We believe that an important role on the long term outcome was played by the age of the overweight and obese groups: a younger age in obese patients has been described in several other studies[7,12,16]. A very large study[17] showed that the groups with higher BMI tend to be younger than those at lower BMI. A better pre-treatment risk profile was also showed in a study including all different type of treatments (TAVI, surgery, balloon valvuloplasty and medical therapy)[18]: again, the overweight and obese patients were younger and had a lower Euroscore and a better LVEF, suggesting that, regardless of the proposed treatment, the overall pre-operative risk of overweight/obese patients seems to be lower than the normal weight and underweight patients. As expected, the higher BMI

groups had a bigger incidence of diabetes and hypertension and it has been demonstrated that obesity is strictly correlated with both these co-morbidities[19,20]. Our study showed that, when adjusted for these co-variates, the relevance of BMI on survival becomes insignificant: BMI appears to be a protective factor only when considered in a univariable analysis. These results support the idea that the obesity paradox in aortic valve replacement is only apparent as mortality rates are mostly affected by co-morbidities and general status of the patient.

Despite several studies aimed to evaluate the impact of BMI on cardiac surgical outcomes, there is not a univocal view on this. In an analysis on valve surgery published in 2012[7], the authors found better survival rates in overweight and obese patients, while a more recent and larger multicentre study found that higher BMI was associated with increased mortality, morbidity and hospital costs[21] after cardiac surgery. Although these studies are large, they frequently involve different type of surgical indications and surgeries; our study was intended to focus only on first time isolated aortic valve replacement procedures: previous retrospective observational studies have specifically focused on this specific operation[8,9,11,12,22], but the majority of them involves heterogenous populations and use different definitions of obesity. In another retrospective study[12] conducted on first time AVR, with or without CABG, BMI was associated with 30-day and long term mortality with a decreased risk observed for patients with BMI in the low 30s compared to patients with BMI in the mid-20s or above 40 kg/m2. In a similar study[9], van Straten and colleagues had comparable results to ours, reporting no correlation between BMI and short term mortality, but also showing a negative correlation between low BMI and the long term survival. In terms of short term outcomes, these were not statistically different between the groups, although it must be noted that the normal weight group had the highest mortality at 30 days. This group had also an higher number of re-sternotomies for bleeding compared to overweight and obese patients, while the highest incidence of DSWI was found in very obese patients: this finding has been already previously demonstrated in a nationwide analysis published in 2017[17] where there was a direct correlation between BMI group and incidence of DSWI.

There are several limitations in this study: first, its retrospective single centre design is certainly limiting its reproducibility. There is also a lack of data on the impact of BMI on non-fatal and non-cardiovascular late adverse events and the underweight group is very small and has been excluded. Moreover, BMI is a dynamic variable that can change over time[23]: some patients might have changed obesity category during follow up

and therefore it is very difficult to evaluate the impact of BMI over time especially with very long term follow up.

In conclusion, we demonstrated that after adjusting for co-morbidities and age, there is no significant protective effect of obesity on long term survival rates after aortic valve replacement for aortic stenosis and therefore an obesity paradox is only apparent in this type of patients. There is a higher incidence of 30 days mortality in the normal weight patients compared to overweight and very obese patients, while an higher incidence of deep sternal wound infections is expected in very obese patients.

References

1. Bastien M, Poirier P, Lemieux I et al. Overview of epidemiology and contribution of obesity to cardiovascular disease. Prog Cardiovasc Dis. 2014;56(4):369-381. doi:10.1016/j.pcad.2013.10.016.

2. Braun N, Gomes F, Schuetz P. “The obesity paradox” in disease - Is the protective effect of obesity true? Swiss Med Wkly. 2015;145(December):1-5. doi:10.4414/smw.2015.14265.

3. Doehner W, Erdmann E, Cairns R, et al. Inverse relation of body weight and weight change with mortality and morbidity in patients with type 2 diabetes and cardiovascular co-morbidity: An analysis of the PROactive study population. Int J Cardiol. 2012;162(1):20-26. doi:10.1016/j.ijcard.2011.09.039.

4. Gonzalez M., Pastore C a., Orlandi SP et al. Obesity paradox in cancer: new insights provided by body composition. Am J Clin Nutr (AM J CLIN NUTR). 2014;99(5):999-1005. doi:<a data-auto="ep_link_" href="http://dx.doi.org.ezproxy.hhs.nl:2048/10.3945/ajcn.113.071399" target="10.3945/ajcn.113.071399" id="linkhttp:dx.doi.org10.3945ajcn.113.071399" title="http://dx.doi.org/10.3945/ajcn.113.071399" data-title="http://dx.doi.org/10.

5. Yamauchi Y, Hasegawa W, Yasunaga H, et al. Paradoxical association between body mass index and in-hospital mortality in elderly patients with chronic obstructive pulmonary disease in Japan. Int J Chron Obstruct Pulmon Dis. 2014:1337. doi:10.2147/COPD.S75175.

6. Antonopoulos AS, Tousoulis D. The molecular mechanisms of obesity paradox. 2017:1074-1086. doi:10.1093/cvr/cvx106.

7. Vaduganathan M, Lee R, Beckham AJ, et al. Relation of body mass index to late survival after valvular heart surgery. Am J Cardiol. 2012;110(11):1667-1678. doi:10.1016/j.amjcard.2012.07.041.

8. Wang B, Yang H, Zhu W et al. Obesity is associated with higher long-term mortality after aortic valve replacement with small prosthesis. Hear Lung Circ. 2013;22(9):731-737. doi:10.1016/j.hlc.2013.03.004.

9. van Straten AHM, Safari M, Ozdemir HI et al. Does the body mass index predict mortality after isolated aortic valve replacement? J Heart Valve Dis. 2013;22(5):608-614. http://www.ncbi.nlm.nih.gov/pubmed/24383370.

10. Mohty D, Dumesnil JG, Echahidi N, et al. Impact of Prosthesis-Patient Mismatch on Long-Term Survival After Aortic Valve Replacement. Influence of Age, Obesity, and Left Ventricular Dysfunction. J Am Coll Cardiol. 2009;53(1):39-47. doi:10.1016/j.jacc.2008.09.022.

11. Smith RL, Herbert MA, Dewey TM, et al. Does body mass index affect outcomes for aortic valve replacement surgery for aortic stenosis? Ann Thorac Surg. 2012;93(3):742-747. doi:10.1016/j.athoracsur.2011.11.027.

12. Roberts WC, Roberts CC, Vowels TJ, et al. Effect of body mass index on survival in patients having aortic valve replacement for aortic stenosis with or without concomitant coronary artery bypass grafting. Am J Cardiol. 2011;108(12):1767-1771. doi:10.1016/j.amjcard.2011.09.010.

13. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894:i-xii, 1-253. http://www.ncbi.nlm.nih.gov/pubmed/11234459.

14. Roques F, Michel P, Goldstone AR et al. The logistic EuroSCORE. Eur Heart J. 2003;24(9):881-882. doi:10.1016/S0195-668X(02)00801-1.

15. Harrell FE. Regression Modeling Strategies. With Applications to Linear Models, Logistic Regression, and Survival Analysis.; 2001. doi:10.1007/978-1-4757-3462-1.

16. Johnson AP, Parlow JL, Whitehead M et al. Body Mass Index, Outcomes, and Mortality Following Cardiac Surgery in Ontario, Canada. J Am Heart Assoc. 2015;4(7):1-13. doi:10.1161/JAHA.115.002140.

17. Mariscalco G, Wozniak MJ, Dawson AG, et al. Body Mass Index and Mortality among Adults Undergoing Cardiac Surgery: A Nationwide Study with a Systematic Review and Meta-Analysis. Circulation. 2017;135(9):850-863. doi:10.1161/CIRCULATIONAHA.116.022840.

18. Rossi A, Gaibazzi N, Bellelli G, et al. Obesity paradox in patients with aortic valve stenosis. Protective effect of body mass index independently of age, disease severity, treatment modality and non-cardiac comorbidities. Int J Cardiol. 2014;176(3):1441-1443. doi:10.1016/j.ijcard.2014.08.037.

19. Hall JE, Do Carmo JM, Da Silva AA et al. Obesity-Induced Hypertension: Interaction of Neurohumoral and Renal Mechanisms. Circ Res. 2015;116(6):991-1006. doi:10.1161/CIRCRESAHA.116.305697.

20. Al-Goblan AS, Al-Alfi MA, Khan MZ. Mechanism linking diabetes mellitus and obesity. Diabetes, Metab Syndr Obes Targets Ther. 2014;7:587-591. doi:10.2147/DMSO.S67400.

21. Ghanta RK, LaPar DJ, Zhang Q, et al. Obesity increases risk-adjusted morbidity, mortality, and cost following cardiac surgery. J Am Heart Assoc. 2017;6(3):1-8. doi:10.1161/JAHA.116.003831.

22. Florath I, Albert AA, Rosendahl UP, et al. Body mass index: a risk factor for 30-day or six-month mortality in patients undergoing aortic valve replacement? J Heart Valve Dis. 2006.

23. Block JP, Subramanian S V., Christakis NA et al. Population Trends and Variation in Body Mass Index from 1971 to 2008 in the Framingham Heart Study Offspring Cohort. PLoS One. 2013;8(5):1-8. doi:10.1371/journal.pone.0063217.

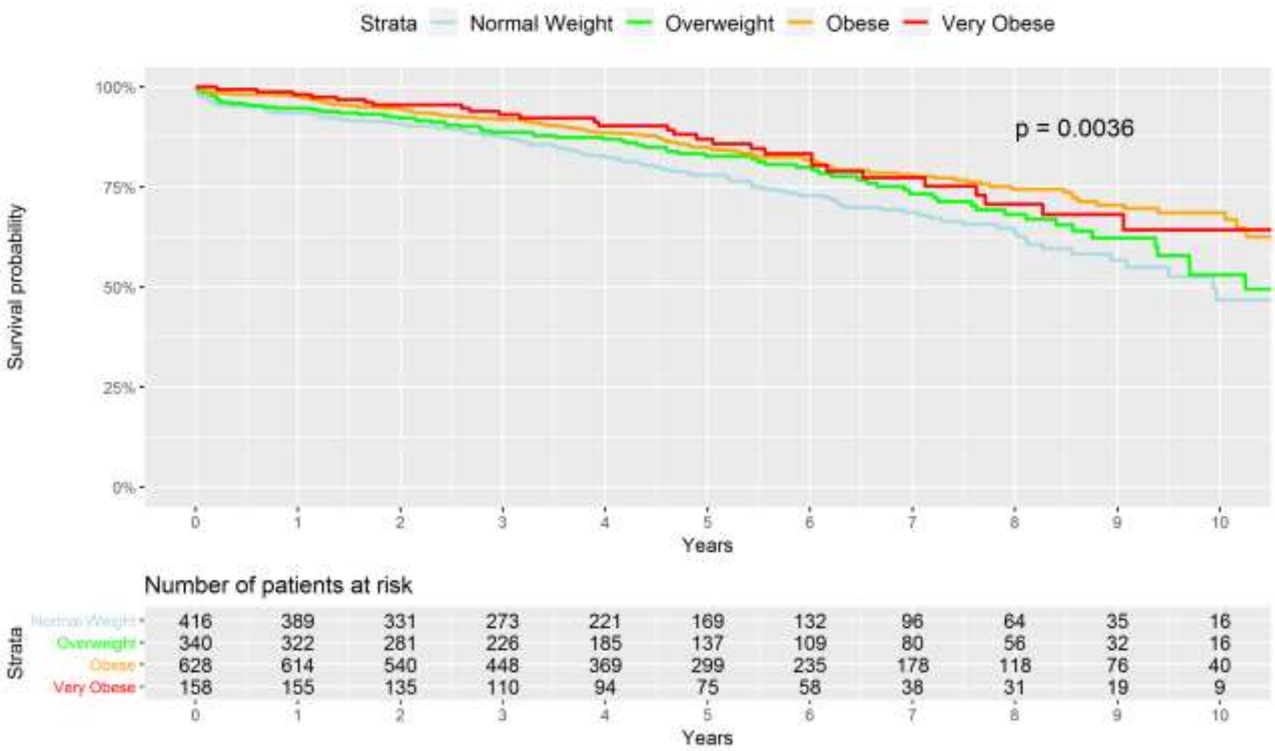

Figure 1. Kaplan-Meier Curve showing the survival rates after surgery stratified for BMI group. BMI: Body mass index.

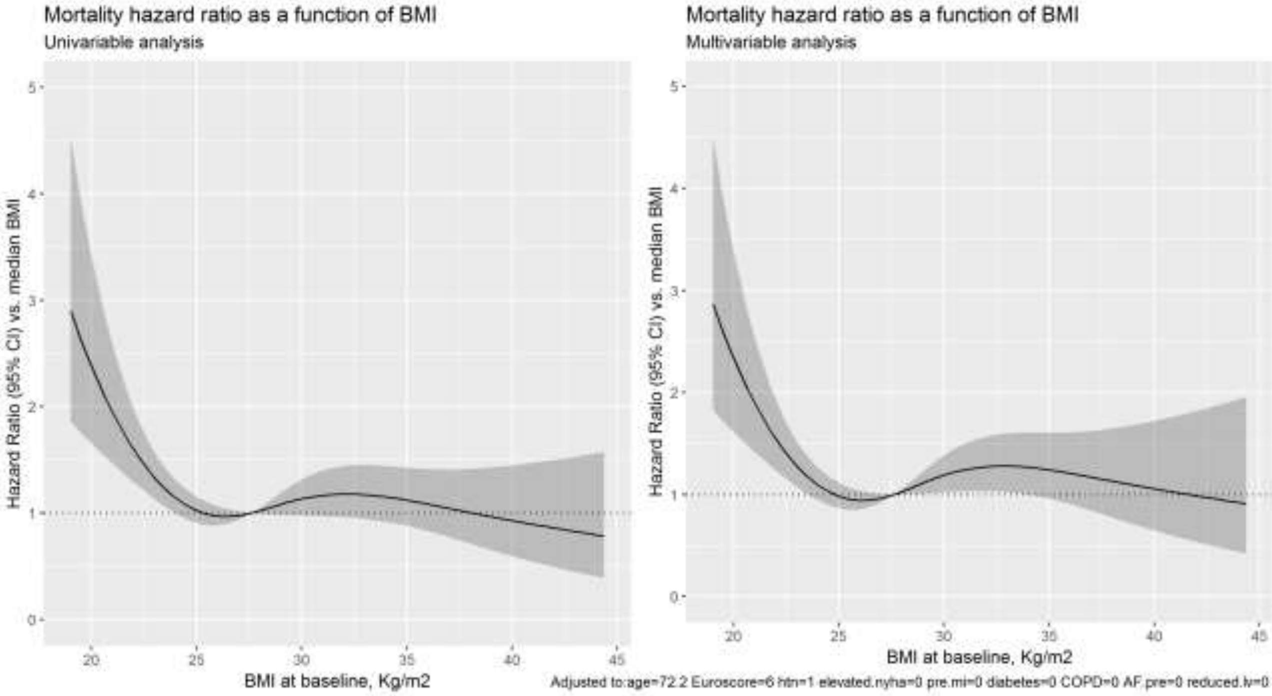

Figure 2. Relationship between body mass index (restricted cubic spline function) and the hazard ratio for late mortality. The univariable analysis is shown on the left side while the multivariable analysis is shown on the right side. Multivariable analysis: prespecified adjustment variables were age, Euroscore, elevated NYHA class, hypertension, diabetes, chronic obstructive pulmonary disease, pre-operative atrial fibrillation and reduced left ventricular function.

Table 1. Preoperative Characteristics

	Body Mass Index Category				
	Normal Weight 418	Overweight 629	Obese 342	Very Obese 158	p-value
BMI (Kg/m2, median [IQR])	22.95 [21.42, 24.15]	27.24 [26.04, 28.53]	32.01 [30.83, 33.30]	37.35 [36.00, 40.60]	<0.001
Age (years, median [IQR])	74.80 [65.53, 80.12]	71.70 [64.60, 78.00]	71.45 [64.20, 76.77]	68.75 [62.75, 74.70]	<0.001
Female Gender (%)	208 (49.8)	239 (38.0)	139 (40.6)	94 (59.5)	<0.001
Hyperthension (%)	208 (49.8)	368 (58.8)	236 (69.4)	118 (75.2)	<0.001
Current Smoker (%)	40 (9.6)	39 (6.2)	14 (4.1)	14 (8.9)	0.016
NYHA class III or IV (%)	166 (39.8)	250 (39.9)	163 (47.8)	98 (62.0)	<0.001
Previous MI (%)	18 (4.3)	34 (5.4)	23 (6.8)	6 (3.8)	0.388
Previous PCI (%)	6 (1.4)	24 (3.8)	10 (2.9)	3 (1.9)	0.123
Diabetes (%)	33 (7.9)	93 (14.8)	69 (20.3)	58 (36.7)	<0.001
IDDM (%)	5 (1.2)	17 (2.7)	10 (2.9)	8 (5.1)	0.065
COPD (%)	61 (14.6)	95 (15.2)	60 (17.6)	32 (20.3)	0.293
Previous Stroke (%)	8 (1.9)	21 (3.3)	18 (5.3)	4 (2.5)	0.075
PVD (%)	17 (4.1)	31 (4.9)	12 (3.5)	7 (4.4)	0.759
Preoperative AF (%)	45 (10.8)	52 (8.3)	35 (10.2)	13 (8.2)	0.486
CAD (%)	20 (5.0)	24 (3.9)	19 (5.7)	2 (1.3)	0.132
Reduced LVEF (%)	75 (18.0)	92 (14.7)	52 (15.3)	31 (19.7)	0.306
Euroscore (median [IQR])	6.00 [4.00, 8.00]	6.00 [4.00, 7.00]	5.00 [4.00, 7.00]	5.00 [4.00, 7.00]	<0.001
Logistic Euroscore (median [IQR])	0.06 [0.03, 0.09]	0.05 [0.03, 0.08]	0.04 [0.03, 0.07]	0.04 [0.03, 0.06]	<0.001

BMI: Body Mass Index; NYHA: New York Heart Association; MI: myocardial infarction; PCI: percutaneous Coronary Intervention; IDDM: Insulin Dependent Diabetes Mellitus; COPD: Chronic Obstructive Pulmonary Disease; PVD: peripheral vascular disease; AF: atrial fibrillation; CAD: coronary artery disease; LVEF: Left ventricualr Ejection Fraction.

Table 2. Operative and postoperative characteristics

	Body Mass Index Category				
	Normal Weight	Overweight	Obese	Very Obese	p-value
	418	629	342	158	
CPB Time (min, median [IQR])	91.00 [75.00, 104.75]	91.00 [78.00, 108.00]	91.00 [78.00, 107.75]	95.00 [82.00, 108.00]	0.079
Cross-clamp time (min, median [IQR])	67.00 [56.00, 78.00]	67.00 [57.00, 80.00]	67.00 [59.00, 79.00]	67.00 [61.00, 79.75]	0.227
30 days Mortality (%)	11 (2.6)	6 (1.0)	5 (1.5)	0 (0.0)	0.054
Resternotomy for bleeding (%)	25 (6.0)	23 (3.7)	11 (3.2)	5 (3.2)	0.169
DSWI (%)	1 (0.2)	2 (0.3)	2 (0.6)	3 (1.9)	0.072
Post-operative CVA (%)	6 (2.7)	10 (2.9)	7 (3.7)	1 (1.2)	0.706
Post-operative Dialysis (%)	5 (2.3)	2 (0.6)	7 (3.7)	2 (2.3)	0.074
LOS (days, median [IQR])	7.00 [6.00, 11.00]	7.00 [6.00, 10.00]	7.00 [6.00, 11.00]	8.00 [6.00, 10.00]	0.792

CPB: cardiopulmonary bypass time; DSWI: deep sternal wound infection; CVA: cerebro-vascular accident; LOS:Length of stay.

Table 3. Results of Cox proportional hazard model for late mortality

	Univariable analysis		**Multivariable analysis**	
Risk Factor	HR (95% CI)	p-value	HR (95% CI)	p-value
BMI Group (Ref: Normal weight)				
Overweight	0.63(0.48-0.81)	<0.01	0.68(0.52-0.89)	0.005
Obese	0.81(0.60-1.09)	0.18	0.93(0.52-0.89)	0.66
Very Obese	0.64(0.42-0.96)	0.03	0.78(0.50-1.22)	0.28
Age	1.08(1.06-1.09)	<0.001	1.06(1.03-1.08)	<0.01
Female gender	0.94(0.76-1.2)	0.593		
Hyperthesion	1.33(1.06-1.67)	0.01	0.94(0.75-1.22)	0.77
Smoker	0.91(0.73-1.14)	0.433		
Diabetes	1.68(1.3-2.2)	<0.001	1.37(1.03-1.81)	0.03
NYHA Class > II	1.93(1.5-2.4)	<0.001	1.30(1.02-1.64)	0.03
Previous MI	1.94(1.30-2.9)	0.001	1.04(0.67-1.62)	0.83
Previous PCI	1.03(0.55-1.92)	0.908		
COPD	1.76(1.36-2.29)	<0.001	1.61(1.20-2.15)	0.013
Previous Stroke	0.75(0.40-1.4)	0.377		
PVD	0.91(0.48-1.71)	0.779		
Pre-operative AF	2.64(1.95-3.53)	<0.001	1.50(1.09-2.07)	0.012
Reduced LVEF	2.2(1.66-2.79)	<0.001	1.49(1.09-2.05)	0.01
Euroscore	1.33(1.27-1.39)	<0.001	1.05(0.95-1.16)	0.77
BMI (linear)	0.97(0.95-0.99)	0.009	0.98(0.96-1.004)	0.12

Definitions: NYHA: New York Heart Association; MI: Myocardial Infarction; PCI: percutaneous coronary intervention; COPD: Chronic Obstructive Pulmonary Disease; PVD: peripheral vascular disease; AF: Atrial Fibrillation; LVEF: Left Ventricular Ejection Fraction; BMI: Body Mass Index.